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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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THOMAS HOXIE
NOVARTIS, CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 430/2
EAST HANOVER, NJ 07936-1080

EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/964,899	COHEN ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- Th MAILING DATE of this communication app ars on the cover she t with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-109* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-109* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-3 and 27-30, drawn to a transgenic fly whose genome comprises a DNA Sequence encoding a polypeptide comprising the Abeta portion of human APP wherein said DNA sequence encodes Abeta40 (SEQ ID NO:1) and methods of using the fly to identify compounds useful for treatment, classified in class 800;800, subclass 3;13.

II. Claims 1-3 and 27-30, drawn to a transgenic fly whose genome comprises a DNA Sequence encoding a polypeptide comprising the Abeta portion of human APP wherein said DNA sequence encodes Abeta42 (SEQ ID NO:2) and methods of using the fly to identify compounds useful for treatment, classified in class 800;800, subclass 3;13.

III. Claims 4-8 and 31-36, drawn to a transgenic fly whose genome comprises a DNA Sequence encoding a polypeptide comprising the wild type C99 portion of human APP (SEQ ID NO:3) and methods using the fly to identify compounds useful for treatment, classified in class 800;800, subclass 3;13.

IV. Claims 4-8 and 31-36, drawn to a transgenic fly whose genome comprises a DNA Sequence encoding a polypeptide comprising the C99 portion of human APP with the London mutation (SEQ ID NO:4) and methods using the fly to identify compounds useful for treatment, classified in class 800;800, subclass 3;13.

V. Claims 9-12, drawn to a method of identifying genetic modifiers using a transgenic fly whose genome comprises a DNA Sequence encoding a polypeptide comprising the Abeta portion of human APP wherein said DNA sequence encodes Abeta40 (SEQ ID NO:1), classified in class 800, subclass 3.

VI. Claims 9-12, drawn to a method of identifying genetic modifiers using a transgenic fly whose genome comprises a DNA Sequence encoding a polypeptide comprising the Abeta portion of human APP wherein said DNA sequence encodes Abeta42 (SEQ ID NO:2) , classified in class 800, subclass 3.

VII. Claims 13-18, drawn to a method of identifying genetic modifiers using a transgenic fly whose genome comprises a DNA Sequence encoding a polypeptide comprising the wild type C99 portion of human APP (SEQ ID NO:3), classified in class 800, subclass 3.

VIII. Claims 13-18, drawn to a method of identifying genetic modifiers using a transgenic fly whose genome comprises a DNA Sequence encoding a polypeptide comprising the C99 portion of human APP with the London mutation (SEQ ID NO:4), classified in class 800, subclass 3.

IX. Claims 19-21, drawn to a method of identifying targets for therapeutics, comprising identifying human homologs of genetic modifiers identified using a transgenic fly comprising the Abeta portion of human APP, classified in class 702, subclass 19.

X. Claims 22-24, drawn to a method of identifying targets for therapeutics, comprising identifying human homologs of genetic modifiers identified using a

transgenic fly comprising a DNA Sequence encoding a polypeptide comprising the C99 portion of human APP, classified in class 702, subclass 19.

XI. Claims 25 and 26, drawn to a method of identifying therapeutic targets comprising identifying genes involved in specific molecular pathways, unclassifiable.

XII. Claim 37, drawn to a method for identifying treatment compounds using a model of Alzheimer's Disease comprising assaying for changes in a homolog of a genetic modifier identified using a transgenic fly comprising the Abeta portion of human APP, classified in class 435;800 subclass 4;3.

XIII. Claim 38, drawn to a method for identifying treatment compounds using a model of Alzheimer's Disease comprising assaying for changes in a homolog of a genetic modifier identified using a transgenic fly comprising the C99 portion of human APP, classified in class 435;800 subclass 4;3.

XIV. Claims 39 and 40, drawn to a method for identifying treatment compounds using a model of Alzheimer's Disease comprising assaying for changes in a homolog of a genetic modifier disclosed in Table 1 classified in class 435;800 subclass 4;3.

XV. Claims 41-44, 54-57 and 68-71 drawn to a method of treating conditions associated with abnormal regulation of the APP pathway using a modulator of a human homolog of a genetic modifier identified using a transgenic fly comprising the Abeta portion of human APP and a pharmaceutical comprising the modulator, classified in class 514;530;530, subclass 2;300;350.

XVI. Claims 45-48, 58-61 and 72-75, drawn to a method of treating conditions associated with abnormal regulation of the APP pathway using a modulator of a human homolog of a genetic modifier identified using a transgenic fly comprising the C99 portion of human APP and a pharmaceutical comprising the modulator, classified in class 514;530;530, subclass 2;300;350.

XVII. Claims 49-53, 62-67 and 76-81 drawn to a method of treating conditions associated with abnormal regulation of the APP pathway using a modulator of a human homolog of a genetic modifier disclosed in Table 1 and a pharmaceutical comprising the modulator, classified in class 514;530;530, subclass 2;300;350.

XVIII. Claims 82, 83 and 90, drawn to a method of treating conditions associated with abnormal regulation of the APP pathway comprising assaying mRNA and/or protein levels of a genetic modifier identified using a transgenic fly comprising the Abeta portion of human APP and administering a substance to treat said condition, classified in class 514;530;530, subclass 2;300;350.

XIX. Claims 84,85 and 91, drawn to a method of treating conditions associated with abnormal regulation of the APP pathway comprising assaying mRNA and/or protein levels of a genetic modifier identified using a transgenic fly comprising the C99 portion of human APP and administering a substance to treat said condition, classified in class 514;530;530, subclass 2;300;350.

XX. Claims 84,85,92 and 93, drawn to a method of treating conditions associated with abnormal regulation of the APP pathway comprising assaying mRNA and/or protein levels of a genetic modifier listed in Table 1 and administering a

substance to treat said condition, classified in class 514;530;530, subclass 2;300;350.

XXI. Claims 94 and 95, drawn to a method of diagnosis comprising measuring mRNA or polypeptides encoded by a genetic modifier identified using a transgenic fly comprising the Abeta portion of human APP, classified in class 435;435, subclass 6;7.14.

XXII. Claims 96 and 97, drawn to a method of diagnosis comprising measuring mRNA or polypeptides encoded by a genetic modifier identified using a transgenic fly comprising the C99 portion of human APP, classified in class 435;435, subclass 6;7.14.

XXIII. Claims 98-101, drawn to a method of diagnosis comprising measuring mRNA or polypeptides encoded by a genetic modifier listed in Table 1, classified in class 435;435, subclass 6;7.14.

XXIV. Claims 102 and 103, drawn to a gene therapy method of treating conditions associated with abnormal regulation of the APP pathway comprising introducing nucleic acids encoding a genetic modifier identified using a transgenic fly comprising the Abeta portion of human APP, classified in class 514, subclass 44.

XXV. Claims 104 and 105, drawn to a gene therapy method of treating conditions associated with abnormal regulation of the APP pathway comprising introducing nucleic acids encoding a genetic modifier identified using a transgenic fly comprising the C99 portion of human APP, classified in class 514, subclass 44.

XXVI. Claims 106-109, drawn to a gene therapy method of treating conditions associated with abnormal regulation of the APP pathway comprising introducing nucleic acids encoding a genetic modifier listed in Table 1, classified in class 514, subclass 44.

If applicants elect either Invention IX, X, XII, XIII, XV or XVI, further restriction will be necessary. These Inventions are drawn to methods of using patentably distinct homologs (Groups IX, X, XII, XIII) or modifiers of homologs (Group XV and XVI), of patentably distinct genetic modifiers identified using patentably distinct transgenic flies. Therefore each of these Groups contains multiple patentably distinct inventions that cannot be determined prior to the identification of the genetic modifiers.

The inventions are distinct, each from the other because of the following reasons:

Inventions I-IV are patentably distinct because the transgenic flies of each invention comprise a different transgene and are materially, structurally and functionally distinct. The phenotype of the flies of each invention is distinct and therefore each has a distinct use. The burden required to search any of Inventions I-IV together would be undue.

Inventions I-IV and each of Inventions V-XIV are patentably distinct because, the transgenic flies can be used to screen for compounds to treat disease conditions while the methods of Inventions V-XI can be used to identify genetic modifiers (Inventions V-VIII) and their human homologs (Inventions IX-XI) and the methods of Invention XII-XIV can be used to identify modulators of a human homolog of a genetic modifier. The protocols and reagents

required for the flies and the methods are materially distinct and separate. The flies do not require the methods and the methods do not require the flies. The burden required to search any of Inventions I-IV together with any of Inventions V-XIV would be undue.

Inventions I-IV and each of Inventions XV-XX and XXIV-XXVI are patentably distinct because, the transgenic flies can be used to screen for compounds to treat disease conditions while the methods of Inventions XV-XVII can be used to treat disease using a modulator of a human homolog of a genetic modifier and the methods of Inventions XVIII-XX can be used to treat disease using a substance that affects a phenotype in an individual with altered levels of a human homolog of a genetic modifier and the methods of Inventions XXIV-XXVI can be used to treat disease by gene therapy using a nucleic acid encoding a genetic modifier. The protocols and reagents required for the flies and the methods are materially distinct and separate. The flies do not require the methods and the methods do not require the flies. The burden required to search any of Inventions I-IV together with any of Inventions XV-XX and XXIV-XXVI would be undue.

Inventions I-IV and each of Inventions XXI-XXIII are patentably distinct because, the transgenic flies can be used to screen for compounds to treat disease conditions while the methods of Inventions XXI-XXIII can be used to diagnose disease. The protocols and reagents required for the flies and the methods are materially distinct and separate. The flies do not require the methods and the methods do not require the flies. The burden required to search any of Inventions I-IV together with any of Inventions XXI-XXIII would be undue.

The methods of inventions V-XXVI are materially different and plurally independent from each other because each is practiced with materially different process steps and technical

considerations and requires materially distinct protocols and reagents. The methods of Inventions V-XI can be used to identify genetic modifiers (Inventions V-VIII) and their human homologs (Inventions IX-XI) and the methods of Invention XII-XIV can be used to identify modulators of a human homolog of a genetic modifier and the methods of Inventions XV-XVII can be used to treat disease using a modulator of a human homolog of a genetic modifier and the methods of Inventions XVIII-XX can be used to treat disease using a substance that affects a phenotype in an individual with altered levels of a human homolog of a genetic modifier, the methods of Inventions XXI-XXIII can be used to diagnose disease and the methods of Inventions XXIV-XXVI can be used to treat disease by gene therapy using a nucleic acid encoding a genetic modifier

The burden required to search any of Inventions V-XXVI together would be undue.

The methods of Inventions V-VIII are materially different and plurally independent from each other because each is practiced with materially different process steps and technical considerations and requires materially distinct protocols and reagents. The methods involve identifying genetic modifiers using patentably distinct transgenic flies. The genetic modifiers identified using different transgenic flies are distinct because they are genetic modifiers of different transgenes. The burden required to search any of Inventions V-VIII together would be undue.

The methods of Inventions IX-XI are materially different and plurally independent from each other because each is practiced with materially different process steps and technical considerations and requires materially distinct protocols and reagents. The methods involve identifying human homologs of patentably distinct genetic modifiers that were identified using

patentably distinct transgenic flies. The genetic modifiers identified using different transgenic flies are distinct because they are genetic modifiers of different transgenes. The burden required to search any of Inventions IX-XI together would be undue.

The methods of Inventions XII-XIV are materially different and plurally independent from each other because each is practiced with materially different process steps and technical considerations and requires materially distinct protocols and reagents. The methods involve identifying modulators of patentably distinct genetic modifiers that were identified using patentably distinct transgenic flies. The genetic modifiers identified using different transgenic flies are distinct. The burden required to search any of Inventions XII-XIV together would be undue.

The methods of Inventions XV-XVII are materially different and plurally independent from each other because each is practiced with materially different process steps and technical considerations and requires materially distinct protocols and reagents. The methods involve methods of treatment using modulators of a human homolog of patentably distinct genetic modifiers that were identified using patentably distinct transgenic flies. The genetic modifiers identified using different transgenic flies are distinct. The burden required to search any of Inventions XV-XVII together would be undue.

The methods of Inventions XVIII-XX are materially different and plurally independent from each other because each is practiced with materially different process steps and technical considerations and requires materially distinct protocols and reagents. The methods involve measuring levels of a genetic modifier that was identified using patentably distinct flies and

administration of a substance to ameliorate a disease condition. The burden required to search any of Inventions XVII-XX together would be undue.

Inventions XXI-XXIII are materially different and plurally independent from each other because each is practiced with materially different process steps and technical considerations and requires materially distinct protocols and reagents. The methods involve methods of diagnosis comprising measuring levels of human homologs of patentably distinct genetic modifiers. The burden required to search any of Inventions XXI-XXIII together would be undue.

Inventions XXIV-XXVI are materially different and plurally independent from each other because each is practiced with materially different process steps and technical considerations and requires materially distinct protocols and reagents. The methods involve using gene therapy to treat a disease comprising administering nucleic acids encoding human homologs of patentably distinct genetic modifiers. The burden required to search any of Inventions XXIV-XXVI together would be undue.

This application contains claims directed to the following patentably distinct species of the claimed invention:

A) hCP50765 (SEQ ID NO: 35),

B) hCP41313 (SEQ ID NO: 15),

C) hCP41313 (SEQ ID NO: 17),

D) hCP41313 (SEQ ID NO: 53),

E) hCP33787 (SEQ ID NO: 41),

F) hCP51594 (SEQ ID NO: 43),

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 25,26, are generic to species A-D and claims 40, 52,53,88,89,93,100,101,108 and 109are generic to species A-F.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Claims 39,49,84,92,98 and 106 are generic to a plurality of disclosed patentably distinct species comprising sequences listed in Table I. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on Mon-Weds 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

PETER PARAS
PATENT EXAMINER

Valarie Bertoglio
Examiner
Art Unit 1632